

## General

### Guideline Title

ESC guidelines for the diagnosis and treatment of acute and chronic heart failure 2012.

### Bibliographic Source(s)

McMurray JJ, Adamopoulos S, Anker SD, Auricchio A, Bohm M, Dickstein K, Falk V, Filippatos G, Fonseca C, Gomez-Sanchez MA, Jaarsma T, Kober L, Lip GY, Maggioni AP, Parkhomenko A, Pieske BM, Popescu BA, Ronnevik PK, Rutten FH, Schwitter J, Seferovic P, Stepinska J, Seferovic P, Trindade PT, Voors AA, Zannad F, Zeiher A, ESC Committee for Practice Guidelines (CPG). ESC guidelines for the diagnosis and treatment of acute and chronic heart failure 2012: the Task Force for the Diagnosis and Treatment of Acute and Chronic Heart Failure 2012 of the European Society of Cardiology. Developed in collaboration with the Heart Failure Association (HFA) of the ESC. Eur Heart J. 2012 Jul;33(14):1787-847. Epub 2012 May 19. [270 references] [PubMed](#)

### Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: Dickstein K, Cohen-Solal A, Filippatos G, McMurray JJ, Ponikowski P, Poole-Wilson PA, Stromberg A, van Veldhuisen DJ, Atar D, Hoes AW, Keren A, Mebazaa A, Nieminen M, Priori SG, Swedberg K, ESC Committee for Practice Guidelines (CPG), Vahanian A, Camm J, De Caterina R, Dean V, Dickstein K, Filippatos G, Funck-Brentano C, Hellemans I, Kristensen SD, McGregor K, Sechtem U, Silber S, Tendera M, Widimsky P, Zamorano JL, Document Reviewers, Tendera M, Auricchio A, Bax J, Bohm M, Corra U, Della Bella P, Elliott PM, Follath F, Gheorghiade M, Hasin Y, Hernborg A, Jaarsma T, Komajda M, Kornowski R, Piepoli M, Prendergast B, Tavazzi L, Vachiery JL, Verheugt FW, Zamorano JL, Zannad F. ESC guidelines for the diagnosis and treatment of acute and chronic heart failure 2008: the Task Force [trunc]. Eur Heart J 2008 Oct;29(19):2388-442.

## Recommendations

### Major Recommendations

The class of recommendations (I-III) and levels of evidence (A-C) are defined at the end of the "Major Recommendations" field.

#### Definition and Diagnosis

##### Diagnosis of Heart Failure

*Recommendations for Diagnostic Investigations in Ambulatory Patients Suspected of Having Heart Failure (HF)\**

#### Investigations to Consider in All Patients

Transthoracic echocardiography is recommended to evaluate cardiac structure and function, including diastolic function, and to measure left ventricular ejection fraction (LVEF) to make the diagnosis of HF, assist in planning and monitoring of treatment, and to obtain prognostic

information. (Class of recommendation I, level of evidence C)

A 12-lead electrocardiogram (ECG) is recommended to determine heart rhythm, heart rate, QRS morphology, and QRS duration, and to detect other relevant abnormalities (see Table 5 in the original guideline). This information also assists in planning treatment and is of prognostic importance. A completely normal ECG makes systolic HF unlikely. (Class of recommendation I, level of evidence C)

Measurement of blood chemistry (including sodium, potassium, calcium, urea/blood urea nitrogen, creatinine/estimated glomerular filtration rate, liver enzymes and bilirubin, ferritin/total iron-binding capacity [TIBC]) and thyroid function is recommended to:

- i. Evaluate patient suitability for diuretic, renin–angiotensin–aldosterone antagonist, and anticoagulant therapy (and monitor treatment)
- ii. Detect reversible/treatable causes of HF (e.g., hypocalcaemia, thyroid dysfunction) and co-morbidities (e.g., iron deficiency)
- iii. Obtain prognostic information

(Class of recommendation I, level of evidence C)

A complete blood count is recommended to:

- i. Detect anaemia, which may be an alternative cause of the patient's symptoms and signs and may cause worsening of HF
- ii. Obtain prognostic information

(Class of recommendation I, level of evidence C)

Measurement of natriuretic peptide (B-type natriuretic peptide [BNP], N-terminal pro B-type natriuretic peptide [NT-proBNP], or mid-regional pro atrial natriuretic peptide [MR-proANP]) should be considered to:

- i. Exclude alternative causes of dyspnoea (if the level is below the exclusion cut-point [see Figure 1 in the original guideline document] HF is very unlikely)
- ii. Obtain prognostic information

(Class of recommendation IIa, level of evidence C)

A chest radiograph (X-ray) should be considered to detect/exclude certain types of lung disease, e.g., cancer (does not exclude asthma/chronic obstructive pulmonary disease [COPD]). It may also identify pulmonary congestion/oedema and is more useful in patients with suspected HF in the acute setting. (Class of recommendation IIa, level of evidence C)

#### Investigations to Consider in Selected Patients

Cardiac magnetic resonance (CMR) imaging is recommended to evaluate cardiac structure and function, to measure LVEF, and to characterize cardiac tissue, especially in subjects with inadequate echocardiographic images or where the echocardiographic findings are inconclusive or incomplete (but taking account of cautions/contraindications to CMR). (Class of recommendation I, level of evidence C)

Coronary angiography is recommended in patients with angina pectoris, who are considered suitable for coronary revascularization, to evaluate the coronary anatomy. (Class of recommendation I, level of evidence C)

Myocardial perfusion/ischaemia imaging (echocardiography, CMR, single-photon emission computed tomography [SPECT], or positron emission tomography [PET]) should be considered in patients thought to have coronary artery disease (CAD), and who are considered suitable for coronary revascularization, to determine whether there is reversible myocardial ischaemia and viable myocardium. (Class of recommendation IIa, level of evidence C)

Left and right heart catheterization is recommended in patients being evaluated for heart transplantation or mechanical circulatory support, to evaluate right and left heart function and pulmonary arterial resistance. (Class of recommendation I, level of evidence C)

Exercise testing should be considered:

- i. To detect reversible myocardial ischaemia
- ii. As part of the evaluation of patients for heart transplantation and mechanical circulatory support
- iii. To aid in the prescription of exercise training
- iv. To obtain prognostic information

(Class of recommendation IIa, level of evidence C)

\*This list is not exhaustive and other investigations are discussed in the original guideline document. Additional investigations may be indicated in patients with suspected acute HF in

the emergency department/hospital, including troponins and D-dimer measurement and right heart catheterization.

## Pharmacological Treatment of Heart Failure with Reduced Ejection Fraction (Systolic Heart Failure)

### Treatments Recommended in Potentially All Patients with Systolic Heart Failure

#### *Pharmacological Treatments Indicated in Potentially All Patients with Symptomatic (New York Heart Association [NYHA] Functional Class II–IV) Systolic Heart Failure*

An angiotensin-converting enzyme (ACE) inhibitor is recommended, in addition to a beta-blocker, for all patients with an ejection fraction (EF)  $\leq 40\%$  to reduce the risk of HF hospitalization and the risk of premature death. (Class of recommendation I, level of evidence A) (CONSENSUS Trial Study Group, 1987; SOLVD Investigators, 1991; Garg & Yusuf, 1995; Packer et al., 1999; "Effect of enalapril on mortality," 1992)

A beta-blocker is recommended, in addition to an ACE inhibitor (or angiotensin receptor blocker [ARB] if ACE inhibitor not tolerated), for all patients with an EF  $\leq 40\%$  to reduce the risk of HF hospitalization and the risk of premature death. (Class of recommendation I, level of evidence A) (The Cardiac Insufficiency Bisoprolol Study II [CIBIS-II], 1999; "Effect of metoprolol CR/XL," 1999; Hjalmarson et al., 2000; Packer et al., 2001; Packer et al., 2002; Flather et al., 2005; Packer et al., "The effect of carvedilol," 1996)

A mineralocorticoid receptor antagonist (MRA) is recommended for all patients with persisting symptoms (NYHA class II–IV) and an EF  $\leq 35\%$ , despite treatment with an ACE inhibitor (or an ARB if an ACE inhibitor is not tolerated) and a beta-blocker, to reduce the risk of HF hospitalization and the risk of premature death. (Class of recommendation I, level of evidence A) (Pitt et al., 1999; Zannad et al., 2011)

#### *Other Treatments with Less-certain Benefits in Patients with Symptomatic (NYHA Class II–IV) Systolic Heart Failure*

### ARB

Recommended to reduce the risk of HF hospitalization and the risk of premature death in patients with an EF  $\leq 40\%$  and unable to tolerate an ACE inhibitor because of cough (patients should also receive a beta-blocker and an MRA). (Class of recommendation I, level of evidence A) (Granger et al., 2003; Maggioni et al., 2002)

Recommended to reduce the risk of HF hospitalization in patients with an EF  $\leq 40\%$  and persisting symptoms (NYHA class II–IV) despite treatment with an ACE inhibitor and a beta-blocker who are unable to tolerate an MRA.\* (Class of recommendation I, level of evidence A) (Cohn & Tognoni, 2001; McMurray et al., 2003)

\*In the CHARM-Added trial, candesartan also reduced cardiovascular mortality.

### Ivabradine

Should be considered to reduce the risk of HF hospitalization in patients in sinus rhythm with an EF  $\leq 35\%$ , a heart rate remaining  $\geq 70$  beats per minute (b.p.m.), and persisting symptoms (NYHA class II–IV) despite treatment with an evidence-based dose of beta-blocker (or maximum tolerated dose below that), ACE inhibitor (or ARB), and an MRA (or ARB).\* (Class of recommendation IIa, level of evidence B) (Swedberg et al., 2010)

May be considered to reduce the risk of HF hospitalization in patients in sinus rhythm with an EF  $\leq 35\%$  and a heart rate  $\geq 70$  b.p.m. who are unable to tolerate a beta-blocker. Patients should also receive an ACE inhibitor (or ARB) and an MRA (or ARB).\* (Class of recommendation IIb, level of evidence C)

\*European Medicines Agency has approved ivabradine for use in patients with a heart rate  $\geq 75$  b.p.m.

### Digoxin

May be considered to reduce the risk of HF hospitalization in patients in sinus rhythm with an EF  $\leq 45\%$  who are unable to tolerate a beta-blocker (ivabradine is an alternative in patients with a heart rate  $\geq 70$  b.p.m.). Patients should also receive an ACE inhibitor (or ARB) and an MRA (or ARB). (Class of recommendation IIb, level of evidence B) (Digitalis Investigation Group, 1997)

May be considered to reduce the risk of HF hospitalization in patients with an EF  $\leq 45\%$  and persisting symptoms (NYHA class II–IV) despite treatment with a beta-blocker, ACE inhibitor (or ARB), and an MRA (or ARB). (Class of recommendation IIb, level of evidence B) (Digitalis Investigation Group, 1997)

### Hydralazine and Isosorbide Dinitrate (H-ISDN)

May be considered as an alternative to an ACE inhibitor or ARB, if neither is tolerated, to reduce the risk of HF hospitalization and risk of premature death in patients with an EF  $\leq 45\%$  and dilated LV (or EF  $\leq 35\%$ ). Patients should also receive a beta-blocker and an MRA. (Class of

recommendation IIb, level of evidence B) (Cohn et al., 1986; Cohn et al., 1991)

May be considered to reduce the risk of HF hospitalization and risk of premature death in patients with an EF  $\leq 45\%$  and dilated LV (or EF  $\leq 35\%$ ) and persisting symptoms (NYHA class II–IV) despite treatment with a beta-blocker, ACE inhibitor (or ARB), and an MRA (or ARB). (Class of recommendation IIb, level of evidence B) (Taylor et al., 2004)

An *n-3* polyunsaturated fatty acid (PUFA) preparation may be considered to reduce the risk of death and the risk of cardiovascular hospitalization in patients treated with an ACE inhibitor (or ARB), beta-blocker, and an MRA (or ARB). (Class of recommendation IIb, level of evidence B) (Gissi-HF Investigators et al., 2008) (Note: preparation studied in cited trial; the GISSI-HF trial had no EF limit.)

Treatments Not Recommended (Believed to Cause Harm)

*Treatments (or Combinations of Treatments) That May Cause Harm in Patients with Symptomatic (NYHA class II–IV) Systolic Heart Failure*

Thiazolidinediones (glitazones) should not be used as they cause worsening HF and increase the risk of HF hospitalization. (Class of recommendation III, level of evidence A) (Komajda et al., 2010; Hernandez et al., 2011; Erdmann et al., 2007)

Most calcium-channel blockers (CCBs) (with the exception of amlodipine and felodipine) are not recommended as they have a negative inotropic effect and can cause worsening HF. (Class of recommendation III, level of evidence B) (Goldstein et al., 1991)

Non-steroidal anti-inflammatory drugs (NSAIDs) and cyclo-oxygenase-2 (COX-2) inhibitors are not recommended as they may cause sodium and water retention, worsening renal function and worsening HF. (Class of recommendation III, level of evidence B) (Mamdani et al., 2004; Huerta et al., 2006)

The addition of an ARB (or renin inhibitor) to the combination of an ACE inhibitor AND a mineralocorticoid antagonist is NOT recommended because of the risk of renal dysfunction and hyperkalaemia. (Class of recommendation III, level of evidence C)

#### Non-surgical Device Treatment of Heart Failure with Reduced Ejection Fraction (Systolic Heart Failure)

Implantable Cardioverter-Defibrillator (ICD)

*Recommendations for the Use of ICDs in Patients with Heart Failure*

#### Secondary Prevention

An ICD is recommended in a patient with a ventricular arrhythmia causing haemodynamic instability, who is expected to survive for  $>1$  year with good functional status, to reduce the risk of sudden death. (Class of recommendation I, level of evidence A) ("A comparison of antiarrhythmic-drug therapy," 1997; Kuck et al., 2000; Connolly et al., 2000; Oseroff, Retyk, & Bochoeyer, 2004)

#### Primary Prevention

An ICD is recommended in a patient with symptomatic HF (NYHA class II–III) and an EF  $\leq 35\%$  despite  $\geq 3$  months of treatment with optimal pharmacological therapy, who is expected to survive for  $>1$  year with good functional status, to reduce the risk of sudden death.

- Ischaemic aetiology and  $>40$  days after acute myocardial infarction (Class of recommendation I, level of evidence A) (Moss et al., 1996; Bardy et al., 2005)
- Non-ischaemic aetiology (Class of recommendation I, level of evidence B) (Bardy et al., 2005)

Cardiac Resynchronization Therapy (CRT)

*Recommendations for the Use of CRT Where the Evidence Is Strong—Patients in Sinus Rhythm with NYHA Functional Class III and Ambulatory Class IV Heart Failure and a Persistently Reduced Ejection Fraction, despite Optimal Pharmacological Therapy*

#### Left Bundle Branch Block (LBBB) QRS Morphology

Cardiac resynchronization therapy-pacemaker (CRT-P)/cardiac resynchronization therapy-defibrillator (CRT-D) is recommended in patients in sinus rhythm with a QRS duration of  $\geq 120$  ms, LBBB QRS morphology, and an EF  $\leq 35\%$ , who are expected to survive with good functional status for  $>1$  year, to reduce the risk of HF hospitalization and the risk of premature death. (Class of recommendation I, level of evidence A) (Bristow et al., 2004; Cleland et al., 2005)

#### Non-LBBB QRS Morphology

CRT-P/CRT-D should be considered in patients in sinus rhythm with a QRS duration of  $\geq 150$  ms, irrespective of QRS morphology, and an EF  $\leq 35\%$ , who are expected to survive with good functional status for  $>1$  year, to reduce the risk of HF hospitalization and the risk of premature death. (Class of recommendation IIa, level of evidence A) (Bristow et al., 2004; Cleland et al., 2005)

*Recommendations for the Use of CRT Where the Evidence Is Strong—Patients in Sinus Rhythm with NYHA Functional Class II Heart Failure and a Persistently Reduced Ejection Fraction, despite Optimal Pharmacological Therapy*

#### LBBB QRS Morphology

CRT, preferably CRT-D is recommended in patients in sinus rhythm with a QRS duration of  $\geq 130$  ms, LBBB QRS morphology, and an EF  $\leq 30\%$ , who are expected to survive for  $>1$  year with good functional status, to reduce the risk of HF hospitalization and the risk of premature death. (Class of recommendation I, level of evidence A) (Moss et al., 2009; Tang et al., 2010)

#### Non-LBBB QRS Morphology

CRT, preferably CRT-D should be considered in patients in sinus rhythm with a QRS duration of  $\geq 150$  ms, irrespective of QRS morphology, and an EF  $\leq 30\%$ , who are expected to survive for  $>1$  year with good functional status, to reduce the risk of HF hospitalization and the risk of premature death. (Class of recommendation IIa, level of evidence A) (Moss et al., 2009; Tang et al., 2010).

*Recommendations for the Use of CRT Where the Evidence Is Uncertain—Patients with Symptomatic HF (NYHA Functional Class II–IV) and a Persistently Reduced EF Despite Optimal Pharmacological Therapy and in Atrial Fibrillation (AF) or with a Conventional Pacing Indication*

#### Patients in Permanent AF

CRT-P/CRT-D should be considered in patients in NYHA functional class III or ambulatory class IV with a QRS duration  $\geq 120$  ms and an EF  $\leq 35\%$ , who are expected to survive with good functional status for  $>1$  year, to reduce the risk of HF worsening if:

- The patient is pacemaker dependent as a result of atrioventricular (AV) nodal ablation (Class of recommendation IIa, level of evidence B) (Ganesan et al., 2012)

CRT-P/CRT-D should be considered in patients in NYHA functional class III or ambulatory class IV with a QRS duration  $\geq 120$  ms and an EF  $\leq 35\%$ , who are expected to survive with good functional status for  $>1$  year, to reduce the risk of HF worsening if:

- The patient requires pacing because of an intrinsically slow ventricular rate (Class of recommendation IIb, level of evidence C)
- The patient's ventricular rate is  $\leq 60$  b.p.m. at rest and  $\leq 90$  b.p.m. on exercise. (Class of recommendation IIb, level of evidence C)

#### Patients with an Indication for Conventional Pacing and No Other Indication for CRT

In patients who are expected to survive with good functional status for  $>1$  year:

- CRT should be considered in those in NYHA functional class III or IV with an EF  $\leq 35\%$ , irrespective of QRS duration, to reduce the risk of worsening of HF (Class of recommendation IIa, level of evidence C)
- CRT may be considered in those in NYHA functional class II with an EF  $\leq 35\%$ , irrespective of QRS duration, to reduce the risk of worsening of HF. (Class of recommendation IIb, level of evidence C)

#### Arrhythmias, Bradycardia, and Atrioventricular Block in Patients with Heart Failure with Reduced Ejection Fraction and Heart Failure with Preserved Ejection Fraction

##### Atrial Fibrillation

*Recommendations for Controlling the Ventricular Rate in Patients with Symptomatic HF (NYHA Functional Class II–IV), LV Systolic Dysfunction, Persistent/Permanent AF and No Evidence of Acute Decompensation*

#### Step 1: A Beta-blocker

A beta-blocker is recommended as the preferred first-line treatment to control the ventricular rate because of the associated benefits of this treatment (reducing the risk of hospitalization for worsening HF and reducing the risk of premature death). (Class of recommendation I, level of evidence A) ("The Cardiac Insufficiency Bisoprolol Study II [CIBIS-II]," 1999; "Effect of metoprolol CR/XL," 1999; Hjalmarson et al., 2000; Packer et al., 2001; Packer et al., 2002; Flather et al., 2005; Packer et al., "The effect of carvedilol," 1996)

### Alternative Step 1 Treatment

- i. Digoxin is recommended in patients unable to tolerate a beta-blocker (Class of recommendation I, level of evidence B) (Digitalis Investigation Group, 1997)
- ii. Amiodarone may be considered in patients unable to tolerate a beta-blocker or digoxin. (Class of recommendation IIb, level of evidence C)
- iii. AV node ablation and pacing (possibly CRT) may be considered in patients unable to tolerate any of a beta-blocker, digoxin, or amiodarone. (Class of recommendation IIb, level of evidence C)

### Step 2: Digoxin

Digoxin is recommended as the preferred second drug, in addition to a beta-blocker, to control the ventricular rate in patients with an inadequate response to a beta-blocker. (Class of recommendation I, level of evidence B) (Digitalis Investigation Group, 1997)

### Alternative Step 2 Treatment

- i. Amiodarone may be considered in addition to either a beta-blocker or digoxin (but not both) to control the ventricular rate in patients with an inadequate response and unable to tolerate the combination of both a beta-blocker and digoxin. (Class of recommendation IIb, level of evidence C)
- ii. AV node ablation and pacing (possibly CRT) may be considered in patients with an inadequate response to two of three of a beta-blocker, digoxin and amiodarone. (Class of recommendation IIb, level of evidence C)

No more than two of three of a beta-blocker, digoxin, and amiodarone (or any other drug suppressing cardiac conduction) should be considered because of the risk of severe bradycardia, third-degree AV block, and asystole. (Class of recommendation IIa, level of evidence C)

### *Recommendations for a Rhythm Control-management Strategy in Patients with AF, Symptomatic HF (NYHA Functional Class II–IV), and LV Systolic Dysfunction and No Evidence of Acute Decompensation*

Electrical cardioversion or pharmacological cardioversion with amiodarone may be considered in patients with persisting symptoms and/or signs of HF, despite optimum pharmacological treatment and adequate control of the ventricular rate, to improve clinical/symptomatic status. (Class of recommendation IIb, level of evidence C)

Amiodarone may be considered prior to (and following) successful electrical cardioversion to maintain sinus rhythm. (Class of recommendation IIb, level of evidence C)

Dronedarone is not recommended because of an increased risk of hospital admissions for cardiovascular causes and an increased risk of premature death. (Class of recommendation III, level of evidence A) (Kober et al., 2008; Connolly et al., 2011)

Class I antiarrhythmic agents are not recommended because of an increased risk of premature death. (Class of recommendation III, level of evidence A) (Echt et al., 1991)

### *Recommendations for the Prevention of Thromboembolism in Patients with Symptomatic HF (NYHA Functional Class II–IV) and Paroxysmal or Persistent/Permanent AF*

The CHA<sub>2</sub>DS<sub>2</sub>-VASc\* and HAS-BLED† scores (see Tables 17 and 18 in the original guideline document) are recommended to determine the likely risk–benefit (thromboembolism prevention versus risk of bleeding) of oral anticoagulation. (Class of recommendation I, level of evidence B) (Lip et al., 2010; Pisters et al., 2010)

An oral anticoagulant is recommended for all patients with paroxysmal or persistent/permanent AF and a CHA<sub>2</sub>DS<sub>2</sub>-VASc\* score  $\geq 1$ , without contraindications, and irrespective of whether a rate- or rhythm-management strategy is used (including after successful cardioversion). (Class of recommendation I, level of evidence A) (Hart et al., 1999)

In patients with AF of  $\geq 48$  h duration, or when the duration of AF is unknown, an oral anticoagulant is recommended at a therapeutic dose for  $\geq 3$  weeks prior to electrical or pharmacological cardioversion. (Class of recommendation I, level of evidence C)

Intravenous heparin or low-molecular-weight heparin (LMWH) is recommended for patients who have not been treated with an anticoagulant and require urgent electrical or pharmacological cardioversion. (Class of recommendation I, level of evidence C)

### Alternative to Intravenous (i.v.) Heparin or LMWH

A transoesophageal echocardiography (TOE)-guided strategy may be considered for patients who have not been treated with an anticoagulant and

require urgent electrical or pharmacological cardioversion. (Class of recommendation IIb, level of evidence C)

Combination of an oral anticoagulant and an antiplatelet agent is not recommended in patients with chronic (>12 months after an acute event) coronary or other arterial disease, because of a high risk of serious bleeding. Single therapy with an oral anticoagulant is preferred after 12 months. (Class of recommendation III, level of evidence A) (Larson & Fisher, 2004)

\*CHA<sub>2</sub>DS<sub>2</sub>-VASc = Cardiac failure, Hypertension, Age ≥75 (Doubled), Diabetes, Stroke (Doubled), Vascular disease, Age 65–74 and Sex category (Female)

†HAS-BLED = Hypertension, Abnormal renal/liver function (1 point each), Stroke, Bleeding history or predisposition, Labile international normalized ratio, Elderly (>65), Drugs/alcohol concomitantly (1 point each).

### *Recommendations for the Management of Ventricular Arrhythmias in Heart Failure*

It is recommended that potential aggravating/precipitating factors (e.g., electrolyte disorders, use of proarrhythmic drugs, myocardial ischaemia) should be sought and corrected in patients with ventricular arrhythmias. (Class of recommendation I, level of evidence C)

It is recommended that treatment with an ACE inhibitor (or ARB), beta-blocker, and MRA should be optimized in patients with ventricular arrhythmias. (Class of recommendation I, level of evidence A) (CONSENSUS Trial Study Group, 1987; SOLVD Investigators, 1991; Garg & Yusuf, 1995; Packer et al., 1999; "Effect of enalapril on mortality," 1992; "The Cardiac Insufficiency Bisoprolol Study II [CIBIS-II]," 1999; "Effect of metoprolol CR/XL," 1999; Hjalmarson et al., 2000; Packer et al., 2001; Packer et al., 2002; Flather et al., 2005; Packer et al., "The effect of carvedilol," 1996; Pitt et al., 1999; Zannad et al., 2011)

It is recommended that coronary revascularization is considered in patients with ventricular arrhythmias and coronary artery disease. (See "Ventricular Dysfunction" in the original guideline document.) (Class of recommendation I, level of evidence C)

It is recommended that an ICD is implanted in a patient with symptomatic or sustained ventricular arrhythmia (ventricular tachycardia or ventricular fibrillation), reasonable functional status, and in whom a goal of treatment is to improve survival. (Class of recommendation I, level of evidence A) ("A comparison of antiarrhythmic-drug therapy," 1997; Kuck et al., 2000; Connolly et al., 2000; Oserooff, Retyk, & Bochoeyer, 2004; Moss et al., 1996; Bardy et al., 2005)

Amiodarone is recommended in patients with an ICD, who continue to have symptomatic ventricular arrhythmias or recurrent shocks despite optimal treatment and device re-programming. (Class of recommendation I, level of evidence C)

Catheter ablation is recommended in patients with an ICD who continue to have ventricular arrhythmias causing recurrent shocks not preventable by optimal treatment device re-programming and amiodarone. (Class of recommendation I, level of evidence C)

Amiodarone may be considered as a treatment to prevent recurrence of sustained symptomatic ventricular arrhythmias in otherwise optimally treated patients in whom an ICD is not considered appropriate. (Class of recommendation IIb, level of evidence C)

Routine use of amiodarone is not recommended in patients with non-sustained ventricular arrhythmias because of lack of benefit and potential drug toxicity. (Class of recommendation III, level of evidence A) (Piepoli et al., 1998; "Effect of prophylactic amiodarone," 1997)

Other antiarrhythmic drugs (particularly class IC agents and dronedarone) should not be used in patients with systolic HF because of safety concerns (worsening HF, proarrhythmia, and death). (Class of recommendation III, level of evidence A) (Kober et al., 2008; Echt et al., 1991)

### Importance and Management of Other Co-morbidity in Heart Failure with Reduced Ejection Fraction and Heart Failure with Preserved Ejection Fraction

#### Angina

*Recommendations for the Pharmacological Treatment of Stable Angina Pectoris in Patients with Symptomatic HF (NYHA Functional Class II–IV) and LV Systolic Dysfunction*

#### Step 1: A Beta-blocker

A beta-blocker is recommended as the preferred first-line treatment to relieve angina because of the associated benefits of this treatment (reducing the risk of HF hospitalization and the risk of premature death). (Class of recommendation I, level of evidence A) ("The Cardiac Insufficiency Bisoprolol Study II [CIBIS-II]," 1999; "Effect of metoprolol CR/XL," 1999; Hjalmarson et al., 2000; Packer et al., 2001; Packer et al., 2002; Flather et al., 2005; Packer et al., "The effect of carvedilol," 1996)

#### Alternatives to a Beta-blocker

- i. Ivabradine should be considered in patients in sinus rhythm who cannot tolerate a beta-blocker, to relieve angina (effective antianginal

treatment and safe in HF). (Class of recommendation IIa, level of evidence A) (Swedberg et al., 2010; Fox et al., 2008)

- ii. An oral or transcutaneous nitrate should be considered in patients unable to tolerate a beta-blocker, to relieve angina (effective antianginal treatment and safe in HF). (Class of recommendation IIa, level of evidence A) (Cohn et al., 1986; Cohn et al., 1991; Taylor et al., 2004)
- iii. Amlodipine should be considered in patients unable to tolerate a beta-blocker, to relieve angina (effective antianginal treatment and safe in HF). (Class of recommendation IIa, level of evidence A) (Packer et al., "Effect of amlodipine," 1996; Wijeyesundera et al., 2003)
- iv. Nicorandil may be considered in patients unable to tolerate a beta-blocker, to relieve angina (effective antianginal treatment but safety in HF uncertain). (Class of recommendation IIb, level of evidence C)
- v. Ranolazine may be considered in patients unable to tolerate a beta-blocker, to relieve angina (effective antianginal treatment but safety in HF uncertain). (Class of recommendation IIb, level of evidence C)

### Step 2: Add a Second Anti-anginal Drug

The following may be added to a beta-blocker (or alternative)—taking account of the combinations not recommended below.

The addition of ivabradine is recommended when angina persists despite treatment with a beta-blocker (or alternative), to relieve angina (effective antianginal treatment and safe in HF). (Class of recommendation I, level of evidence A) (Swedberg et al., 2010; Fox et al., 2008)

The addition of an oral or transcutaneous nitrate is recommended when angina persists despite treatment with a beta-blocker (or alternative), to relieve angina (effective antianginal treatment and safe in HF). (Class of recommendation I, level of evidence A) (Cohn et al., 1986; Cohn et al., 1991; Taylor et al., 2004)

The addition of amlodipine is recommended when angina persists despite treatment with a beta-blocker (or alternative), to relieve angina (effective antianginal treatment and safe in HF). (Class of recommendation I, level of evidence A) (Packer et al., "Effect of amlodipine," 1996; Wijeyesundera et al., 2003)

The addition of nicorandil may be considered when angina persists despite treatment with a beta-blocker (or alternative), to relieve angina (effective antianginal treatment but safety in HF uncertain). (Class of recommendation IIb, level of evidence C)

The addition of ranolazine may be considered when angina persists despite treatment with a beta-blocker (or alternative), to relieve angina (effective antianginal treatment but safety in HF uncertain). (Class of recommendation IIb, level of evidence C)

### Step 3: Coronary Revascularization

Coronary revascularization is recommended when angina persists despite treatment with two antianginal drugs. (Class of recommendation I, level of evidence A) (Yusuf et al., 1994; Velazquez et al., 2011)

Alternatives to coronary revascularization: A third antianginal drug from those listed above may be considered when angina persists despite treatment with two antianginal drugs (excluding the combinations not recommended below). (Class of recommendation IIb, level of evidence C)

The following are NOT recommended:

- Combination of any of ivabradine, ranolazine, and nicorandil because of unknown safety (Class of recommendation III, level of evidence C)
- Combination of nicorandil and a nitrate (because of lack of additional efficacy) (Class of recommendation III, level of evidence C)

Diltiazem or verapamil are not recommended because of their negative inotropic action and risk of worsening HF (Class of recommendation III, level of evidence B) (Goldstein et al., 1991)

## Hypertension

*Recommendations for the Treatment of Hypertension in Patients with Symptomatic HF (NYHA Functional Class II–IV) and LV Systolic Dysfunction*

### Step 1

One or more of an ACE inhibitor (or ARB), beta-blocker, and MRA is recommended as first-, second-, and third-line therapy, respectively, because of their associated benefits (reducing the risk of HF hospitalization and reducing the risk of premature death). (Class of recommendation I, level of evidence A) (CONSENSUS Trial Study Group, 1987; Granger et al., 2003; Maggioni et al., 2002; Cohn & Tognoni, 2001; McMurray et al., 2003)

### Step 2



A thiazide diuretic (or if the patient is treated with a thiazide diuretic, switching to a loop diuretic) is recommended when hypertension persists despite treatment with a combination of as many as possible of an ACE inhibitor (or ARB), beta-blocker, and MRA. (Class of recommendation I, level of evidence C)

### Step 3

Amlodipine is recommended when hypertension persists despite treatment with a combination of as many as possible of an ACE inhibitor (or ARB), beta-blocker, MRA, and diuretic. (Class of recommendation I, level of evidence A) (Packer et al., "Effect of amlodipine," 1996; Wijesundera et al., 2003)

Hydralazine is recommended when hypertension persists despite treatment with a combination of as many as possible of an ACE inhibitor (or ARB), beta-blocker, MRA, and diuretic. (Class of recommendation I, level of evidence A) (Cohn et al., 1986; Cohn et al., 1991; Taylor et al., 2004)

Felodipine should be considered when hypertension persists despite treatment with a combination of as many as possible of an ACE inhibitor (or ARB), beta-blocker, MRA, and diuretic. (Class of recommendation IIa, level of evidence B) (Cohn et al., 1997)

Moxonidine is NOT recommended because of safety concerns (increased mortality). (Class of recommendation III, level of evidence B) (Cohn et al., 2003)

Alpha-adrenoceptor antagonists are NOT recommended because of safety concerns (neurohumoral activation, fluid retention, worsening HF). (Class of recommendation III, level of evidence A) ("Major cardiovascular events," 2000; Dorszewski et al., 1997; Bayliss et al., 1985)

### Acute Heart Failure

#### Treatment of Acute Heart Failure

#### *Recommendations for the Treatment of Patients with Acute Heart Failure*

#### Patients with Pulmonary Congestion/Oedema without Shock

An i.v. loop diuretic is recommended to improve breathlessness and relieve congestion. Symptoms, urine output, renal function, and electrolytes should be monitored regularly during use of i.v. diuretic. (Class of recommendation I, level of evidence B) (Felker et al., 2011)

High-flow oxygen is recommended in patients with a capillary oxygen saturation <90% or partial pressure of arterial oxygen (PaO<sub>2</sub>) <60 mmHg (8.0 kPa) to correct hypoxaemia. (Class of recommendation I, level of evidence C)

Thromboembolism prophylaxis (e.g., with LMWH) is recommended in patients not already anticoagulated and with no contraindication to anticoagulation, to reduce the risk of deep venous thrombosis and pulmonary embolism. (Class of recommendation I, level of evidence A) (Alikhan et al., 2003; Kleber et al., 2003; Tebbe et al., 2011)

Non-invasive ventilation (e.g., continuous positive airway pressure [CPAP]) should be considered in dyspnoeic patients with pulmonary oedema and a respiratory rate >20 breaths/min to improve breathlessness and reduce hypercapnia and acidosis. Non-invasive ventilation can reduce blood pressure and should not generally be used in patients with a systolic blood pressure <85 mmHg (and blood pressure should be monitored regularly when this treatment is used). (Class of recommendation IIa, level of evidence B) (Gray et al., 2008)

An i.v. opiate (along with an antiemetic) should be considered in particularly anxious, restless, or distressed patients to relieve these symptoms and improve breathlessness. Alertness and ventilatory effort should be monitored frequently after administration because opiates can depress respiration. (Class of recommendation IIa, level of evidence C)

An i.v. infusion of a nitrate should be considered in patients with pulmonary congestion/oedema and a systolic blood pressure >110 mmHg, who do not have severe mitral or aortic stenosis, to reduce pulmonary capillary wedge pressure and systemic vascular resistance. Nitrates may also relieve dyspnoea and congestion. Symptoms and blood pressure should be monitored frequently during administration of i.v. nitrates. (Class of recommendation IIa, level of evidence B) (Cotter et al., 1998; Publication Committee for the VMAC Investigators [Vasodilatation in the Management of Acute CHF], 2002)

An i.v. infusion of sodium nitroprusside may be considered in patients with pulmonary congestion/oedema and a systolic blood pressure >110 mmHg, who do not have severe mitral or aortic stenosis, to reduce pulmonary capillary wedge pressure and systemic vascular resistance. Caution is recommended in patients with acute myocardial infarction. Nitroprusside may also relieve dyspnoea and congestion. Symptoms and blood pressure should be monitored frequently during administration of i.v. nitroprusside. (Class of recommendation IIb, level of evidence B) (Cohn et

al., 1982)

Inotropic agents are NOT recommended unless the patient is hypotensive (systolic blood pressure <85 mmHg), hypoperfused, or shocked because of safety concerns (atrial and ventricular arrhythmias, myocardial ischaemia, and death). (Class of recommendation III, level of evidence C)

#### Patients with Hypotension, Hypoperfusion or Shock

Electrical cardioversion is recommended if an atrial or ventricular arrhythmia is thought to be contributing to the patient's haemodynamic compromise in order to restore sinus rhythm and improve the patient's clinical condition. (Class of recommendation I, level of evidence C)

An i.v. infusion of an inotrope (e.g., dobutamine) should be considered in patients with hypotension (systolic blood pressure <85 mmHg) and/or hypoperfusion to increase cardiac output, increase blood pressure, and improve peripheral perfusion. The ECG should be monitored continuously because inotropic agents can cause arrhythmias and myocardial ischaemia. (Class of recommendation IIa, level of evidence C)

Short-term mechanical circulatory support should be considered (as a 'bridge to recovery') in patients remaining severely hypoperfused despite inotropic therapy and with a potentially reversible cause (e.g., viral myocarditis) or a potentially surgically correctable cause (e.g., acute interventricular septal rupture). (Class of recommendation IIa, level of evidence C)

An i.v. infusion of levosimendan (or a phosphodiesterase inhibitor) may be considered to reverse the effect of beta-blockade if beta-blockade is thought to be contributing to hypoperfusion. The electrocardiogram (ECG) should be monitored continuously because inotropic agents can cause arrhythmias and myocardial ischaemia, and, as these agents are also vasodilators, blood pressure should be monitored carefully. (Class of recommendation IIb, level of evidence C)

A vasopressor (e.g., dopamine or norepinephrine) may be considered in patients who have cardiogenic shock, despite treatment with an inotrope, to increase blood pressure and vital organ perfusion. The ECG should be monitored as these agents can cause arrhythmias and/or myocardial ischaemia. Intra-arterial blood pressure measurement should be considered. (Class of recommendation IIb, level of evidence C)

Short-term mechanical circulatory support may be considered (as a 'bridge to decision') in patients deteriorating rapidly before a full diagnostic and clinical evaluation can be made. (Class of recommendation IIb, level of evidence C)

#### Patients with an Acute Coronary Syndrome (ACS)

Immediate primary percutaneous coronary intervention (PCI) (or coronary artery bypass graft [CABG] in selected cases) is recommended if there is an ST elevation or a new LBBB ACS in order to reduce the extent of myocyte necrosis and reduce the risk of premature death. (Class of recommendation I, level of evidence A) (Mehta et al., 2005)

Alternative to PCI or CABG: Intravenous thrombolytic therapy is recommended, if PCI/CABG cannot be performed, if there is ST-segment elevation or new LBBB, to reduce the extent of myocyte necrosis and reduce the risk of premature death. (Class of recommendation I, level of evidence A) (Fibrinolytic Therapy Trialists' [FTT] Collaborative Group, 1994)

Early PCI (or CABG in selected patients) is recommended if there is non-ST elevation ACS in order to reduce the risk of recurrent ACS. Urgent revascularization is recommended if the patient is haemodynamically unstable. (Class of recommendation I, level of evidence A) (Mehta et al., 2005)

Eplerenone is recommended to reduce the risk of death and subsequent cardiovascular hospitalization in patients with an EF  $\leq$ 40%. (Class of recommendation I, level of evidence B) (Pitt et al., 2003)

An ACE inhibitor (or ARB) is recommended in patients with an EF  $\leq$ 40%, after stabilization, to reduce the risk of death, recurrent myocardial infarction, and hospitalization for HF. (Class of recommendation I, level of evidence A) (Flather et al., 2000)

A beta-blocker is recommended in patients with an EF  $\leq$ 40%, after stabilization, to reduce the risk of death and recurrent myocardial infarction. (Class of recommendation I, level of evidence B) (Dargie, 2001)

An i.v. opiate (along with an antiemetic) should be considered in patients with ischaemic chest pain to relieve this symptom (and improve breathlessness). Alertness and ventilatory effort should be monitored frequently after administration because opiates can depress respiration. (Class of recommendation IIa, level of evidence C)

#### Patients with AF and a Rapid Ventricular Rate

Patients should be fully anticoagulated (e.g., with i.v. heparin), if not already anticoagulated and with no contraindication to anticoagulation, as soon

as AF is detected to reduce the risk of systemic arterial embolism and stroke. (Class of recommendation I, level of evidence A) (Hart et al., 1999)

Electrical cardioversion is recommended in patients haemodynamically compromised by AF and in whom urgent restoration of sinus rhythm is required to improve the patient's clinical condition rapidly. (Class of recommendation I, level of evidence C)

Electrical cardioversion or pharmacological cardioversion with amiodarone should be considered in patients when a decision is made to restore sinus rhythm non-urgently ('rhythm control' strategy). This strategy should only be employed in patients with a first episode of AF of <48 h duration (or in patients with no evidence of left atrial appendage thrombus on TOE). (Class of recommendation I, level of evidence C)

Intravenous administration of a cardiac glycoside should be considered for rapid control of the ventricular rate. (Class of recommendation I, level of evidence C)

Dronedarone is not recommended because of safety concerns (increased risk of hospital admission for cardiovascular causes and an increased risk of premature death), particularly in patients with an EF  $\leq$ 40%. (Class of recommendation III, level of evidence A) (Kober et al., 2008)

Class I antiarrhythmic agents are not recommended because of safety concerns (increased risk of premature death), particularly in patients with LV systolic dysfunction. (Class of recommendation III, level of evidence A) (Echt et al., 1991)

#### *Patients with Severe Bradycardia or Heart Block*

Pacing is recommended in patients haemodynamically compromised by severe bradycardia or heart block to improve the patient's clinical condition. (Class of recommendation I, level of evidence C)

#### Coronary Revascularization and Surgery, Including Valve Surgery, Ventricular Assist Devices, and Transplantation

##### Coronary Revascularization

##### *Recommendations for Myocardial Revascularization in Patients with Chronic HF and Systolic LV Dysfunction*

CABG is recommended for patients with angina and significant left main stenosis, who are otherwise suitable for surgery and expected to survive >1 year with good functional status, to reduce the risk of premature death. (Class of recommendation I, level of evidence C)

CABG is recommended for patients with angina and two- or three-vessel coronary disease, including a left anterior descending stenosis, who are otherwise suitable for surgery and expected to survive >1 year with good functional status, to reduce the risk of hospitalization for cardiovascular causes and the risk of premature death from cardiovascular causes. (Class of recommendation I, level of evidence B) (Velazquez et al., 2011)

Alternative to CABG: PCI may be considered as an alternative to CABG in the above categories of patients unsuitable for surgery. (Class of recommendation IIb, level of evidence C)

CABG and PCI are NOT recommended in patients without angina AND without viable myocardium. (Class of recommendation III, level of evidence C)

##### Mechanical Circulatory Support

##### *Recommendations for Surgical Implantation of Left Ventricular Assist Devices (LVADs) in Patients with Systolic Heart Failure*

An LVAD or bi-ventricular assist device (BiVAD) is recommended in selected patients (see sections 13.5.1 and 13.5.2 and Table 25 in the original guideline document) with end-stage HF despite optimal pharmacological and device treatment and who are otherwise suitable for heart transplantation, to improve symptoms and reduce the risk of HF hospitalization for worsening HF and to reduce the risk of premature death while awaiting transplantation. (Class of recommendation I, level of evidence B) (Rose et al., 2001; Slaughter et al., 2009; Pagani et al., 2009)

An LVAD should be considered in highly selected patients who have end-stage HF despite optimal pharmacological and device therapy and who are not suitable for heart transplantation, but are expected to survive >1 year with good functional status, to improve symptoms, and reduce the risk of HF hospitalization and of premature death. (Class of recommendation IIa, level of evidence B) (Rose et al., 2001)

#### Holistic Management, Including Exercise Training and Multidisciplinary Management Programmes, Patient Monitoring, and Palliative Care

##### Recommendations for Exercise Prescription and Multidisciplinary Management

It is recommended that regular aerobic exercise is encouraged in patients with heart failure to improve functional capacity and symptoms. (Class of recommendation I, level of evidence A) (O'Connor et al., 2009; Piepoli et al., 2011)

It is recommended that patients with heart failure are enrolled in a multidisciplinary-care management programme to reduce the risk of heart failure hospitalization. (Class of recommendation I, level of evidence A) (McDonagh et al., 2011; Lainscak et al., 2011; Sochalski et al., 2009)

#### Definitions:

#### Levels of Evidence

<b>Level of Evidence A</b>	Data derived from multiple randomized clinical trials or meta-analyses.
<b>Level of Evidence B</b>	Data derived from a single randomized clinical trial or large non-randomized studies.
<b>Level of Evidence C</b>	Consensus of opinion of the experts and/or small studies, retrospective studies, registries.

#### Classes of Recommendations

<b>Classes of Recommendations</b>	<b>Definition</b>	<b>Suggested Wording to Use</b>
<b>Class I</b>	Evidence and/or general agreement that a given treatment or procedure is beneficial, useful, effective.	Is recommended/is indicated
<b>Class II</b>	Conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of the given treatment or procedure.	
<b>Class IIa</b>	<i>Weight of evidence/opinion is in favour of usefulness/efficacy.</i>	Should be considered
<b>Class IIb</b>	<i>Usefulness/efficacy is less well established by evidence/opinion.</i>	May be considered
<b>Class III</b>	Evidence or general agreement that the given treatment or procedure is not useful/effective, and in some cases may be harmful.	Is not recommended

## Clinical Algorithm(s)

The following clinical algorithms are provided in the original guideline document:

- Diagnostic flowchart for patients with suspected heart failure—showing alternative 'echocardiography first' (blue) or 'natriuretic peptide first' (red) approaches
- Treatment options for patients with chronic symptomatic systolic heart failure (NYHA functional class II–IV)
- Recommendations for controlling the ventricular rate in patients with heart failure and persistent/permanent atrial fibrillation and no evidence of acute decompensation
- Initial assessment of patient with suspected acute heart failure
- Algorithm for management of acute pulmonary oedema/congestion

## Scope

### Disease/Condition(s)

Chronic heart failure

### Other Disease/Condition(s) Addressed

- Angina
- Atrial fibrillation
- Hypertension
- Ventricular arrhythmias

## Guideline Category

Diagnosis

Evaluation

Management

Risk Assessment

Treatment

## Clinical Specialty

Cardiology

Critical Care

Emergency Medicine

Family Practice

Geriatrics

Internal Medicine

Pulmonary Medicine

## Intended Users

Advanced Practice Nurses

Health Care Providers

Nurses

Pharmacists

Physician Assistants

Physicians

## Guideline Objective(s)

- To provide practical, evidence-based guidelines for the diagnosis and treatment of acute and chronic heart failure
- To assist physicians in selecting the best management strategies for an individual patient with a given condition, taking into account the impact on outcome, as well as the risk–benefit ratio of particular diagnostic or therapeutic means

## Target Population

Adults with acute or chronic heart failure

## Interventions and Practices Considered

Diagnosis/Evaluation

1. Transthoracic echocardiography (assessment of left ventricular systolic and diastolic dysfunction)

2. Transoesophageal echocardiography
3. 12-lead electrocardiogram (ECG)
4. Routine laboratory tests (blood chemistry, thyroid function, full blood count)
5. Measurement of natriuretic peptides
6. Chest X-ray
7. Cardiac magnetic resonance (CMR) imaging
8. Coronary angiography
9. Single-photon emission computed tomography (SPECT) and radionuclide ventriculography
10. Positron emission tomography (PET) imaging
11. Cardiac catheterization

## Management/Treatment

1. Pharmacological treatment of heart failure with reduced ejection fraction (systolic heart failure)
  - Angiotensin-converting enzyme inhibitors and beta-blockers
  - Angiotensin receptor blockers
  - Mineralocorticoid receptor antagonists
  - Ivabradine
  - Digoxin
  - Hydralazine and isosorbide dinitrate
  - n-3 polyunsaturated fatty acids
2. Avoidance of thiazolidinediones, most calcium channel blockers, non-steroidal anti-inflammatory drugs (NSAIDs) and cyclooxygenase-2 inhibitors
3. Diuretics
4. Non-surgical device treatment of heart failure with reduced ejection fraction (systolic heart failure)
  - Implantable cardioverter-defibrillator
  - Cardiac resynchronization therapy
5. Management of arrhythmias, bradycardia, and atrioventricular block
6. Management of other comorbidities (thromboembolism, stable angina pectoris, hypertension)
7. Management of acute heart failure
8. Coronary revascularization and surgery, including valve surgery, ventricular assist devices, and transplantation
9. Holistic management, including exercise training and multidisciplinary management programmes, patient monitoring, and palliative care

Note: See the original guideline document for other interventions that were considered but for which no specific recommendations were made.

## Major Outcomes Considered

- Sensitivity, accuracy, utility of diagnostic tests for heart failure
- Overall mortality
- Cardiovascular hospitalization
- Re-hospitalization
- Survival
- Symptom improvement
- Quality of life

## Methodology

### Methods Used to Collect/Select the Evidence

Searches of Electronic Databases

### Description of Methods Used to Collect/Select the Evidence

PubMed, Ovid MedLine, EMBASE, the Cochrane Library, the US Food and Drug Administration website, ClinicalTrials.gov, National Institute for Health and Clinical Excellence (NICE), National Health Service (NHS) Evidence, National Guideline Clearinghouse, and Centres for Reviews and Dissemination databases were searched without time restriction, although the searches focused primarily on the period between the last and current publications. Non-human studies were excluded.

Specific search terms included heart failure, cardiac failure, ventricular failure, cardiac insufficiency, ventricular dysfunction, pulmonary oedema/edema, cardiomyopathy, arrhythmias, echocardiography, natriuretic peptides, ejection fraction, renin-angiotensin system, beta-blockers, cardiac resynchronisation/resynchronization, implantable cardioverter defibrillator, digitalis, transplantation, heart transplant, cardiac transplant, heart transplantation, cardiac transplantation, ventricular assist device, left ventricular assist device, mechanical circulatory support, bridge, bridging.

## Number of Source Documents

Not stated

## Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

## Rating Scheme for the Strength of the Evidence

Levels of Evidence

Level of Evidence A	Data derived from multiple randomized clinical trials or meta-analyses.
Level of Evidence B	Data derived from a single randomized clinical trial or large non-randomized studies.
Level of Evidence C	Consensus of opinion of the experts and/or small studies, retrospective studies, registries.

## Methods Used to Analyze the Evidence

Review of Published Meta-Analyses

Systematic Review

## Description of the Methods Used to Analyze the Evidence

Selected experts in the field undertook a comprehensive review of the published evidence for diagnosis, management, and/or prevention of a given condition according to the European Society of Cardiology Committee for Practice Guidelines (CPG) policy. A critical evaluation of diagnostic and therapeutic procedures was performed including assessment of the risk–benefit ratio. Estimates of expected health outcomes for larger populations were included, where data exist. The level of evidence and the strength of recommendation of particular treatment options were weighed and graded according to pre-defined scales (see the "Rating Scheme for the Strength of the Evidence" and the "Rating Scheme for the Strength of the Recommendations" fields).

## Methods Used to Formulate the Recommendations

Expert Consensus

## Description of Methods Used to Formulate the Recommendations

Members of this Task Force were selected by the European Society of Cardiology (ESC) to represent professionals involved with the medical care of patients with this pathology. Selected experts in the field undertook a comprehensive review of the published evidence for diagnosis,

management, and/or prevention of a given condition according to ESC Committee for Practice Guidelines (CPG) policy.

## Rating Scheme for the Strength of the Recommendations

### Classes of Recommendations

Classes of Recommendations	Definition	Suggested Wording to Use
<b>Class I</b>	Evidence and/or general agreement that a given treatment or procedure is beneficial, useful, effective.	Is recommended/is indicated
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<b>Class III</b>	Evidence or general agreement that the given treatment or procedure is not useful/effective, and in some cases may be harmful.	Is not recommended

## Cost Analysis

A formal cost analysis was not performed and published cost analyses were not reviewed.

## Method of Guideline Validation

External Peer Review

Internal Peer Review

## Description of Method of Guideline Validation

The European Society of Cardiology (ESC) Guidelines undergo extensive review by the Committee for Practice Guidelines (CPG) and external experts. After appropriate revisions, it is approved by all the experts involved in the Task Force. The finalized document is approved by the CPG for publication in the *European Heart Journal*.

## Evidence Supporting the Recommendations

### References Supporting the Recommendations

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## Type of Evidence Supporting the Recommendations

The type of supporting evidence is identified and graded for each recommendation (see the "Major Recommendations" field).

## Benefits/Harms of Implementing the Guideline Recommendations

### Potential Benefits

Appropriate diagnosis and treatment of acute and chronic heart failure

### Potential Harms

- Angiotensin-converting enzyme (ACE) inhibitors occasionally cause worsening of renal function, hyperkalaemia, symptomatic hypotension,

cough, and, rarely, angioedema. An ACE inhibitor should only be used in patients with adequate renal function (creatinine  $\leq 221$  mmol/L or  $\leq 2.5$  mg/dL or estimated glomerular filtration rate [eGFR]  $\geq 30$  mL/min/1.73 m<sup>2</sup>) and a normal serum potassium level.

- The most common adverse effects with hydralazine and isosorbide dinitrate (H-ISDN) in trials were headache, dizziness/hypotension, and nausea. Arthralgia leading to discontinuation or reduction in dose of H-ISDN occurred in 5% to 10% of patients in V-HeFT I and II and a sustained increase in antinuclear antibody in 2% to 3% of patients (but lupus-like syndrome was rare).
- The main adverse effects of n-3 polyunsaturated fatty acids (PUFAs) reported in these trials were nausea and other minor gastrointestinal disturbances.
- Spironolactone can also cause breast discomfort and enlargement in men (10% compared with 1% on placebo, in RALES); this side effect is infrequent with eplerenone.
- In one study, 5% of patients on ivabradine had symptomatic bradycardia compared with 1% of the placebo group ( $P < 0.0001$ ). Visual side effects (phosphenes) were reported by 3% of patients on ivabradine and 1% on placebo ( $P < 0.0001$ ).
- The main side effects of intravenous vasodilators are hypotension, headache, isocyanate toxicity, tolerance on continuous use, and light sensitivity.
- Inotropes cause sinus tachycardia and may induce myocardial ischaemia and arrhythmias. There is long-standing concern that they may increase mortality.
- Opiates induce nausea (necessitating the concomitant administration of an antiemetic, one of which, cyclizine, has vasoconstrictor activity) and depress respiratory drive, potentially increasing the need for invasive ventilation.
- Digoxin can cause atrial and ventricular arrhythmias, particularly in the context of hypokalaemia, and serial monitoring of serum electrolytes and renal function is mandatory.
- Dopamine may cause hypoxaemia. Arterial oxygen saturation should be monitored, and supplemental oxygen administered as required.
- Patients should be counselled as to the purpose of an ICD and the complications related to its use (predominantly inappropriate shocks).
- Apart from the shortage of donor hearts, the main challenges in transplantation are the consequences of the limited effectiveness and complications of immunosuppressive therapy in the long term (i.e., antibody-mediated rejection, infection, hypertension, renal failure, malignancy, and coronary artery vasculopathy).

See also Web Tables 11, 12, 13, and 14 in the guidelines Addenda for additional cautions, adverse effects, drug interactions, advice, and problem-solving related to use of angiotensin-converting enzyme inhibitors, angiotensin II receptor blockers, beta-blockers, mineralocorticoid receptor antagonists, and diuretics (see the "Availability of Companion Documents" field).

## Contraindications

### Contraindications

- Some new anticoagulant drugs such as the oral direct thrombin inhibitors and oral factor Xa inhibitors are contraindicated in severe renal impairment (creatinine clearance  $< 30$  mL/min).
- Beta-blockers are contraindicated in asthma but not in chronic obstructive pulmonary disease (COPD), although a selective beta-1 adrenoceptor antagonist (i.e., bisoprolol, metoprolol succinate, or nebivolol) is preferred.
- Contraindications to heart transplantation
  - Active infection
  - Severe peripheral arterial or cerebrovascular disease
  - Current alcohol and/or drug abuse
  - Treated cancer in previous 5 years
  - Unhealed peptic ulcer
  - Recent thromboembolism
  - Significant renal failure (e.g., creatinine clearance  $< 50$  mL/min)
  - Significant liver disease
  - Systemic disease with multiorgan involvement
  - Other serious co-morbidity with a poor prognosis
  - Emotional instability or untreated mental illness
  - High, fixed pulmonary vascular resistance ( $> 4\text{--}5$  Wood Units and mean transpulmonary gradient  $> 15$  mmHg)
- Contraindications include hypotension, vomiting, possible pneumothorax, and depressed consciousness.
- Oxygen should not be used routinely in non-hypoxaemic patients as it causes vasoconstriction and a reduction in cardiac output.
- Colchicine should not be used in patients with very severe renal dysfunction and may cause diarrhoea.

- Negatively inotropic calcium channel blockers (CCBs) (i.e., diltiazem and verapamil) should not be used to treat hypertension in patients with heart failure with reduced ejection fraction (HF-REF) (but are believed to be safe in heart failure with preserved ejection fraction [HF-PEF]), and moxonidine should also be avoided in patients with HF-REF as it increased mortality in patients in one randomized controlled trial (RCT).

See Section 7.4 in the original guideline document for treatments not recommended (believed to cause harm). See also Web Tables 11, 12, 13, and 14 in the guidelines Addenda for additional contraindications related to use of angiotensin-converting enzyme inhibitors, angiotensin II receptor blockers, beta-blockers, mineralocorticoid receptor antagonists, and diuretics (see the "Availability of Companion Documents" field).

## Qualifying Statements

### Qualifying Statements

- The European Society of Cardiology (ESC) Guidelines represent the view of the ESC and were arrived at after careful consideration of the available evidence at the time they were written. Health professionals are encouraged to take them fully into account when exercising their clinical judgment. The Guidelines do not, however, override the individual responsibility of health professionals to make appropriate decisions in the circumstance of the individual patients, in consultation with that patient, and where appropriate and necessary the patient's guardian or carer. It is also the health professional's responsibility to verify the rules and regulations applicable to drugs and devices at the time of prescription.
- Guidelines are no substitutes, but are complements, for textbooks and cover the ESC Core Curriculum topics. Guidelines and recommendations should help physicians to make decisions in their daily practice. However, the final decisions concerning an individual patient must be made by the responsible physician(s).

## Implementation of the Guideline

### Description of Implementation Strategy

The task of developing European Society of Cardiology (ESC) Guidelines covers not only the integration of the most recent research, but also the creation of educational tools and implementation programmes for the recommendations. To implement the guidelines, condensed pocket guidelines versions, summary slides, booklets with essential messages, and an electronic version for digital applications (smartphones, etc.) are produced. These versions are abridged and, thus, if needed, one should always refer to the full text version which is freely available on the ESC website. The National Societies of the ESC are encouraged to endorse, translate, and implement the ESC Guidelines. Implementation programmes are needed because it has been shown that the outcome of disease may be favourably influenced by the thorough application of clinical recommendations.

Surveys and registries are needed to verify that real-life daily practice is in keeping with what is recommended in the guidelines, thus completing the loop between clinical research, writing of guidelines, and implementing them into clinical practice.

### Implementation Tools

Clinical Algorithm

Foreign Language Translations

Pocket Guide/Reference Cards

Staff Training/Competency Material

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.



# Categories

## IOM Care Need

End of Life Care

Getting Better

Living with Illness

## IOM Domain

Effectiveness

Patient-centeredness

# Identifying Information and Availability

## Bibliographic Source(s)

McMurray JJ, Adamopoulos S, Anker SD, Auricchio A, Bohm M, Dickstein K, Falk V, Filippatos G, Fonseca C, Gomez-Sanchez MA, Jaarsma T, Kober L, Lip GY, Maggioni AP, Parkhomenko A, Pieske BM, Popescu BA, Ronnevik PK, Rutten FH, Schwitter J, Seferovic P, Stepinska J, Seferovic P, Trindade PT, Voors AA, Zannad F, Zeiher A, ESC Committee for Practice Guidelines (CPG). ESC guidelines for the diagnosis and treatment of acute and chronic heart failure 2012: the Task Force for the Diagnosis and Treatment of Acute and Chronic Heart Failure 2012 of the European Society of Cardiology. Developed in collaboration with the Heart Failure Association (HFA) of the ESC. Eur Heart J. 2012 Jul;33(14):1787-847. Epub 2012 May 19. [270 references] [PubMed](#)

## Adaptation

Not applicable: The guideline was not adapted from another source.

## Date Released

2005 (revised 2012 Jul)

## Guideline Developer(s)

European Society of Cardiology - Medical Specialty Society

Heart Failure Association of the ESC - Disease Specific Society

## Guideline Developer Comment

Not applicable

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# Guideline Committee

Task Force for the Diagnosis and Treatment of Acute and Chronic Heart Failure 2012

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The experts of the writing and reviewing panels filled in declarations of interest forms of all relationships which might be perceived as real or potential sources of conflicts of interest. These forms were compiled into one file and can be found on the [European Society of Cardiology \(ESC\) Web site](#) . Any changes in declarations of interest that arise during the writing period must be notified to the ESC and updated.

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## Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: Dickstein K, Cohen-Solal A, Filippatos G, McMurray JJ, Ponikowski P, Poole-Wilson PA, Stromberg A, van Veldhuisen DJ, Atar D, Hoes AW, Keren A, Mebazaa A, Nieminen M, Piori SG, Swedberg K, ESC Committee for Practice Guidelines (CPG), Vahanian A, Camm J, De Caterina R, Dean V, Dickstein K, Filippatos G, Funck-Brentano C, Hellems I, Kristensen SD, McGregor K, Sechtem U, Silber S, Tendera M, Widimsky P, Zamorano JL, Document Reviewers, Tendera M, Auricchio A, Bax J, Bohm M, Corra U, Della Bella P, Elliott PM, Follath F, Gheorghiade M, Hasin Y, Hemborg A, Jaarsma T, Komajda M, Komowski R, Piepoli M, Prendergast B, Tavazzi L, Vachieri JL, Verheugt FW, Zamorano JL, Zannad F. ESC guidelines for the diagnosis and treatment of acute and chronic heart failure 2008: the Task Force [trunc]. Eur Heart J 2008 Oct;29(19):2388-442.

## Guideline Availability

Electronic copies: Available from the [European Society of Cardiology \(ESC\) Web site](#) . Also available in [Spanish](#)  and [Turkish](#)  from the ESC Web site.

Print copies: Available from Oxford University Press, Great Clarendon Street, Oxford, OX2 6DP, UK, Tel: +44 (0) 1865 353263, Fax: +44 (0) 1865 353774, Web site: <http://www.eurheartj.oxfordjournals.org/> .

## Availability of Companion Documents

The following are available:

- ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure 2012. Addenda. 2012. 8 p. Electronic copies: Available in Portable Document Format (PDF) from the [European Society of Cardiology \(ESC\) Web site](#) .
- ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure 2012. Corrigendum. 2013. 1 p. Electronic copies: Available in Portable Document Format (PDF) from the [ESC Web site](#) .
- Acute and chronic heart failure. Pocket guidelines. Available for order from the [ESC Web site](#) .

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## Patient Resources

None available

## NGC Status

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